II. REMARKS

Formal Matters

Claims 15, 18, 21, and 68 are pending after entry of the amendments set forth herein.

Claims 15, 17, 18, 21, and 68 were examined and were rejected.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Withdrawn rejection

Applicants note with gratitude that the rejection of claims 15, 17, 18, 21, and 66 under 35 U.S.C. §102(e) over Sturley (U.S. Patent No. 6,100,077; "Sturley"), raised in the Office Action mailed March 8,

Rejection under 35 U.S.C. §103(a)

Claims 15, 17, 18, 21, and 68 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Sturley.

The Office Action stated that: 1) Sturley teaches a human diacylglycerol acyltransferase (DGAT) having the amino acid sequence of SEQ ID NO:1; 2) SEQ ID NO:1 of Sturley is 100% identical to SEQ ID NO:6 of the instant application; 3) Sturley teaches methods for identifying a chemical compound that is capable of inhibiting DGAT, comprising contacting DGAT with the chemical and detecting a change in enzymatic activity of the DGAT compared to a control; and 4) the taught method include the introduction of the candidate agent into a cell that includes the DGAT polypeptide and the detection of incorporation of [14C]-oleate into sterol ester.

The Office Action concluded that one of ordinary skill in the art would have been motivated to identify a chemical compound that is capable of inhibiting DGAT. Applicants respectfully traverse the rejection.

As noted previously, and as acknowledged by the Office, Sturley does not teach an *in vitro* screening assay for determining a candidate agent's DGAT inhibitory activity, the method comprising contacting a DGAT polypeptide with the candidate agent; and detecting a change in DGAT enzymatic activity of the DGAT polypeptide compared to a control, where the detecting comprises detecting **incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor**. Sturley's discussion of detection of incorporation of [14C]-oleate into the sterol cholesterol **is not** incorporation of

a detectably labeled fatty acyl CoA into a diacylglycerol. As discussed previously, [14C]-oleate is not a fatty acyl CoA; and cholesterol is not a diacylglycerol.

The Office Action stated:

> potential pharmaceutical composition for the treatment of atherosclerosis. The taught methods include the introduction of said candidate agent into a cell that includes said DGAT polypeptide. Such methods of measuring diacylglycerol activity comprise detecting incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor as well as detecting incorporation of a fatty acyl CoA into a detectably labeled diacylglycerol acceptor and measuring using TLC. The expectation of success is high

Office Action, page 4.

However, Sturley does not teach any such methods. Sturley does not teach "measuring diacylglycerol activity" by "detecting incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor" or "detecting incorporation of a fatty acyl CoA into a detectably labeled diacylglycerol acceptor and measuring using TLC."

There is simply no teaching in Sturley that the polypeptide of SEQ ID NO:1 is a DGAT. At most, Sturley teaches that it is not an ACAT. Sturley speculates that the polypeptide of SEQ ID NO:1 might possess DGAT activity; however, the only rationale for such speculation is a "predicted possession of a diacylglycerol/phorbol ester binding site." Sturley, column 21, lines 21-24. Sturley states that "ARGP1 likely catalyzes a reaction similar to ACAT"; and states that "Other esterification reactions which use fatty-acyl CoAs as substrates include retinol esterification, methyl ester formation, tripterpene esterification, monoacylglycerol transferase, and diacylglycerol transferase." Sturley, column 23, lines 4-9. Thus, Sturley does not provide any hard evidence as to what the enzymatic activity of the polypeptide of SEQ ID NO:1 is. All Sturley shows is that the polypeptide of SEQ ID NO:1 is not an ACAT. Sturley speculates that the polypeptide of SEQ ID NO:1 might possess an activity "similar to ACAT" and lists five different possible esterification reactions, only one of which is DGAT. Without the knowledge provided in the instant application, namely that the polypeptide of SEQ ID NO:6 possesses DGAT activity, there would be no real reason for a person skilled in the art to consider that

the polypeptide of SEQ ID NO:6 would carry out any particular one of the five esterification reactions speculated to be possible activities for the polypeptide of SEQ ID NO:6. As such, Sturley cannot render any of claims 15, 17, 18, 21, and 68 obvious.

Conclusion as to the rejections under 35 U.S.C. §103(a)

Applicants submit that the rejection of claims 15, 17, 18, 21, and 68 under 35 U.S.C. §103(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-105CIP2.

Respectfully submitted,
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Date: Oct. 30, 2007

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